Price, availability and affordability of antineoplastic medicines in Harare's public and private institutions: Implications for access

By

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PREFACE

This dissertation is presented in an article format. The findings of the study are presented in manuscript format as required by the regulations of the University of KwaZulu-Natal. A complete reference list is included at the end of the thesis and presented according to the reference style of the University of KwaZulu-Natal.

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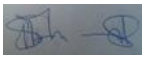
Signature  Date 1st July, 2020

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I, Sly Ngoni Mutyavaviri, declare that:

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This is to certify that the contents of this thesis are the original work of Mr Sly Ngoni Mutyavaviri and as the candidate's co-supervisor, I have approved this thesis for submission.

Signed: 

Name: Dr Amos Marume Date: 1st July 2020

This is to certify that the contents of this thesis are the original work of Mr Sly Ngoni Mutyavaviri and as the candidate's supervisor, I have approved this thesis for submission.

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Name: Dr Varsha Bangalee Date: 1st July 2020

DECLARATION 2 – MANUSCRIPT PUBLICATION

- The manuscript was submitted to the BMC Public Health- Journal, Submission I.D PUBH-D-19-04160

1. My contribution to the project was as follows:

Sly Ngoni Mutyavaviri: Author - contributed to the project by performing all literature reviews, data collection and statistical analyses, interpretation of the results as well as manuscript preparation and writing of dissertation.

2. The contributions of others to the project were as follows:

Dr. Varsha Bangalee: Supervisor - supervision of the concept of the study and writing of the dissertation and manuscript.

Dr. Amos Marume: Co-supervisor - supervision of the concept of the study and writing of the dissertation and manuscript.

DEDICATION

I dedicate this work to the Mutyavaviri family for always believing in me and for your support throughout this project.

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I wish to also thank all the pharmacists in Zimbabwe and the pharmacy and hospital staff at Parirenyatwa Hospital, Harare Hospital and Chitungwiza Hospital that participated in the study.

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LIST OF ACRONYMS AND ABBREVIATIONS

GDP	Gross Domestic Product
HIV/AIDS	Human Infectious Virus/ Acquired Immune Deficiency Syndrome
MRP	Median Price Ratio
NCPCS	National Cancer Prevention and Control Strategy
UNDP	United Nations Development Fund
RTGS	Real Time Gross Settlement
VEN	Vital Essential Necessary list of medicines
WHO/HAI	World Health Organisation/ Health Action Initiative

Abstract

Background: Antineoplastic medicines are increasingly becoming more vital in many public health setups. There has been significant progress made in terms of newer molecules since the advent of chemotherapy. Despite the importance of antineoplastic medicines and advent of these molecules, there are still issues of limited availability and affordability in Zimbabwe. Currently the country has no government initiated policies on pricing and accessibility of antineoplastic medicines in public and private institutions, placing health care consumers at risk. A study was therefore designed to assess the price, availability and affordability of antineoplastic medicines in Harare Province, Zimbabwe.

Methods: The study was based on the standardised method recommended by the World Health Organisation (WHO) and Health Action International (HAI). A data collection form-based cross-sectional survey was conducted in public and private medicine outlets. A total of 153 facilities were surveyed. The facilities consisted of three (3) public institutions and one hundred and fifty (150) private pharmacies in Harare and surrounding towns. The percentage availability, median price ratio using International Reference Prices, mark-ups, price and affordability of antineoplastic medicines were determined. Affordability was determined by using the wage of the lowest paid government worker which was USD296 per month.

Median price ratios were calculated for twenty-two (22) of the antineoplastic medicines that were imported into the country from the import records at the Medicines Control Authority and also appearing on the medicines register for private pharmacies and seven (7) medicines for the public hospital pharmacies. The WHO's International Reference Prices were used for calculation of median price ratios. Range, mode and average mark-up percentages for the antineoplastic medicines were also determined. Availability and price in the public sector was compared to availability in the private sector. Affordability was calculated as the out-of-pocket day's wages to buy a monthly cycle of the antineoplastic medicine.

Results: The percentage availability of the antineoplastic medicines at the government institutions was 25%, whilst the percentage availability of the antineoplastic medicines in the private sector ranged from 1% to 42.7%. Fifty percent of the twenty-two (22) medicines in the private sector had a median price ratio of lower than 4. The median price ratio in the private sector ranged from 0.60 to 11. Median price ratios were calculated for seven (7) medicines in the public sector. The median price ratio in the public sector ranged from 0.73 to 2.25. Eleven

(11) of the medicines in the private sector were affordable with ten (10) days wage and below. Eight of the medicines were slightly affordable with wage days more than 10 days wage but less than 20 days wage. Wage days in private sector ranged from 1 day to 490 days. Affordability of the medicines in the public sector ranged from 1 to 10 days wage. Average percentage mark-up was 51.3% in the private sector and 34% in the public sector for the medicines that were available.

Conclusion: Medicines were generally more available in the private sector than in the public sector. The government needs to continue supporting the National Pharmaceutical Company's procurement of antineoplastic medicines. Generally medicines were more affordable in the public sector than in the private sector. The high percentage mark-ups calculated in the private sector compared to the public sector are as a result of the overhead expenses in private pharmacies which have to be borne from the actual sales of the medicines unlike in the public sector were the services are subsidised by the government. The low availability of antineoplastic medicines coupled with a very high unemployment rate means there is a huge burden on accessibility of antineoplastic medicines in Harare. Most patients cannot afford antineoplastic medicines which can result in increased mortality. There is a need to subsidise the medicines to improve accessibility. This will reduce the out-of-pocket expenses made by patients. There is a need to also ensure that medical insurance in Zimbabwe allow all pharmacies to retail antineoplastic medicines instead of the selective incorporation of pharmacies into their health insurance schemes. The calculated median price ratios range showed that the prices of the medicines are varied and there is need to have medicine procurement and pricing policies that minimise the median price ratio to lower than 5 for all antineoplastic medicines.

Keywords: Affordability, antineoplastic medicines, availability, Zimbabwe

CHAPTER 1 INTRODUCTION

Division of chapters

The dissertation consists of four chapters as follows:

- Chapter 1: Provides an introduction to the study as well as the aims, objectives and a brief overview of the methodology.
- Chapter 2: Provides the literature background to the study.
- Chapter 3: Presents the findings of the study.
- Chapter 4: Consists of the discussion of the study, recommendations, limitations and strengths of the study.
- Chapter 5: Consists of the conclusion of the study.

1.0 Introduction

This chapter explores the background and context of the study. This chapter discusses the current situation in Zimbabwe and how it affects the availability and affordability of antineoplastic medicines. The chapter discusses the rationale, aims and objectives and methodology used to address the research objectives in the study.

1.1 Background and context of the study

One of the Millennium Development Goals (MDGs) acknowledges the need to improve the availability of affordable medicines for all people in developing countries (WHO/HAI, 2008). This goal has been adopted into goal number 3 on good health well-being of the Sustainable Development Goals (United Nations, 2015). Many initiatives have been put in place through the Global Fund, which mainly looks into three major diseases namely, HIV/AIDS, malaria and tuberculosis. However there has not been much attention on other critical non-communicable diseases like cancer. There is no or little availability of antineoplastic medicines in all institutions through donor initiatives as is the case with the aforementioned conditions (National Cancer Prevention and Control Strategy, 2014).

Currently in Zimbabwe there is no essential medicines list that incorporates the antineoplastic medicines in detail. The 7th Edition of the Essential Medicines List in Zimbabwe has no standard detailed approach on how to manage specific types of cancers (National Medicines

Therapeutics Advisory Committee, 2015). This lack of standard therapy leads to variability in treatment approaches.

There is a high possibility that with the current economic crunch, most medicines are beyond the reach of many, as the majority of people are living below the poverty datum line which was USD 596 for a family of five people, as of August 2018 (ZIMSTATS, 2018). With an incidence rate of almost 5000 per year, the current cancer treatment and palliation services are unable to meet the existing demand for services (National Cancer Prevention and Control Strategy, 2014). According to the National Cancer Control Program for Zimbabwe, some of the challenges that were identified included funding constraints which have resulted from cancer being low on the funding agenda. According to Mendis *et al*. (2007), patients with chronic diseases such as cardiovascular disease, diabetes, asthma amongst others require a reliable supply of affordable medicines. In the absence of such a supply, avoidable mortality and morbidity will occur (Mendis et al., 2007).

The environment in Zimbabwe is currently unregulated when it comes to pricing of medicines, which can negatively impact the availability and affordability of essential medicines, antineoplastic medicines being amongst them (Gavaza, 2009). The National Cancer Prevention strategy indicated that chemotherapy was very expensive and scarce in public institutions. The only option for patients was to use out-of-pocket funds to access those medicines (National Cancer Prevention and Control Strategy, 2014). Use of out-of-pocket funds results in low accessibility as most people in Zimbabwe are currently unemployed and they are living below the poverty datum line (ZIMSTATS, 2018).

The availability of medicines has worsened with the introduction of the bond note, which is a surrogate currency that was introduced by the government of Zimbabwe through Statutory Instrument S.I. 133 of 2016 (Government of Zimbabwe, 2016). The bond note is supposed to be at par with the United States Dollar (USD), which is the official currency in Zimbabwe. However there has been unavailability of the USD to allocate to pharmaceutical companies for importation of essential medicines. This has negatively impacted the availability of medicines (The Standard Newspaper, 2018). An unofficial exchange rate now exists between the USD and the bond notes. This means that the general public will access medicines at an inflated unofficial price.

1.1.1 Rationale for study

According to the National Cancer Prevention and Control Strategy (NCPCS), there is a need for population-wide, integrated and cohesive approach to cancer that encompasses prevention, screening, diagnosis, treatment and support, palliative and rehabilitative care (National Cancer Strategy, 2014). Hence a study that assesses the price, accessibility and availability of antineoplastic medicines is warranted as it would indicate the economic burden and accessibility issues which may be used to guide policy implementation. The study will give a quantifiable number that indicates the affordability of antineoplastic medicines, which would be of paramount importance for future planning.

According to the WHO/HAI on MDGs, little data was available on the mark-ups applied to the cost of production of medicines as they move through the supply and distribution chains (World Health Organisation, 2008). There is a need for studies that would show the current mark-up prices and pricing structures of antineoplastic medicines and how these affect accessibility and availability. The NCPCS document stated that there had not been reliable or consistent documentation of most elements of cancer treatment in Zimbabwe (National Cancer Strategy, 2014).

The government has continued to blame the players in the pharmaceutical sector for selling medicines in foreign currency at the expense of the patients (The Standard, 2018). This has been worsened by the need to source the United States Dollars by the pharmaceutical players to support the private health care demand of medicines (The Standard Newspaper, 2018). The study will explore the issues affecting the supply chain and the mark-ups and comparison of the selling price to the global market through the median price ratios.

Zimbabwe as a country has been relying on the importation of antineoplastic medicines from countries like India, South Africa and other European countries (Medicines Control Authority of Zimbabwe, 2018). There has been rationing in the allocation of foreign currency to wholesalers for importation of essential medicines from foreign manufacturers who also manufacture antineoplastic medicines. The failure by local wholesalers to import medicines has resulted in shortages of essential medicines. However, the extent of this shortage is unknown. Hence the need to do a study that can detail the reduction in the importation of registered products and how this has impacted price and affordability on individuals who now have to rely on special importation through the ‘Section 75’ process of the Medicines and

Allied Substances Control Act that provides for importation of unregistered medicines by retail pharmacies in Zimbabwe (Medicines Control Authority of Zimbabwe, 2018).

1.1.2 Definition of terminology

- Medicines accessibility - having medicines continuously available and affordable at public or private health facilities or medicines outlets that are within one hour's walk from the homes of the population (WHO, 2018).
- Essential medicines- are medicines that satisfy the priority health care need of the population (WHO, 2005)
- Affordability -the number of days' wages for the lowest paid government worker. The affordability is then expressed as the number of day's wages to buy a course of the medicine in a month (WHO, 2018)

To facilitate international comparisons, medicine prices found during the survey are expressed as ratios relative to a standard set of international reference prices, known as the median price ratio (MPR). The ratio is an expression of how much greater or less the median local medicine price is than the international reference price, e.g. an MPR of 2 would mean that the local medicine price is twice the international reference price (WHO/HAI, 2008)

1.1.3 Antineoplastic medicines registration status in Zimbabwe

The Medicines Control Authority of Zimbabwe (MCAZ) registers, licenses and/or controls manufacture, wholesaling, dispensing and importation of all medicines. The government institutions import their medicines through the government wholesaler which is the National Pharmaceutical Company, whilst the private institutions rely mostly on the approved wholesalers in Zimbabwe. Of the seven (7) manufacturing facilities in Zimbabwe, none manufacture antineoplastic medicines (MCAZ, 2018). The country relies mainly on generic imports from other countries. The government has also put in place through the Medicines and Allied Substances Control Act, a special importation called 'Section 75', which provides for the bulk importation of unregistered essential medicines (MCAZ, 2018).

1.2 Research Questions

1.2.1 What are the prices of antineoplastic medicines in Zimbabwe?

1.2.2 What are the percentage mark-ups of antineoplastic medicines in Zimbabwe's private and public sector?

1.2.3 What is the percentage availability of antineoplastic medicines in the public and private sectors?

1.2.4 Are antineoplastic medicines affordable to the general public in Zimbabwe?

1.3 Aims & Objectives

1.3.1 Aims

The aim of this research is to determine the price, availability and affordability of antineoplastic medicines in Harare's public and private health institutions in order to guide policy formulation that can aid availability and accessibility of antineoplastic medicines.

1.3.2 Objectives

The objectives of the study are as follows:

(i) To determine the price of antineoplastic medicines in Harare's public and private health institutions.
(ii) To determine the percentage availability of antineoplastic medicines.
(iii) To determine the affordability of antineoplastic medicines.
(iv) To determine if there are variations in availability, acquisition price and affordability between the public and private sectors.
(v) To determine the price mark-ups of the antineoplastic medicine.
(vi) To determine the median price ratio by comparing the prices of the antineoplastic medicines in Harare against the current International Reference Prices

1.4 Significance and novelty of work

The findings of the study have a bearing on a number of government policies such as the registration status for the antineoplastic medicines, lobbying for a cancer levy and subsidised importation of antineoplastic medicines. The identified price issues like price and mark-ups can be used to lobby for such policies as price controls and fixed mark-ups. The National Cancer Preventative Control Strategy, lobbied for studies that can result in greater understanding of the availability and affordability of antineoplastic medicines. This study will contribute to that understanding.

According to the study by the WHO, essential medicines that satisfy the priority health care needs of the population are the backbone of health care and well-being of individuals. Access to essential medicines is a fundamental right (WHO, 2004). There has been significant blame shift in the pharmaceutical industry, with the retailers being accused of profiteering. A study of this nature will demystify some of these beliefs and facilitate ease of dialogue amongst all the players in the pharmaceutical industry (The Standard, 2018). The study will also demonstrate the probable challenges that cancer patients have been facing when it comes to accessing medicines.

The median price ratios will also demonstrate the financial challenges that are faced by the local importers. There is a need for the government to capacitate the local industry so that there is a reduction on importation of antineoplastic medicines. This is only feasible if there is evidence based information that demonstrates the availability and price issues surrounding the antineoplastic medicines.

1.5 Research methodology

1.5.1 Study design

Study type: Quantitative cross-sectional descriptive survey.

1.5.1.1 Study setting

The study was conducted in Harare the capital city of Zimbabwe and the surrounding small towns. Harare has a nearby town called Chitungwiza which is 25km away from the Central Business District.

1.5.1.2 Study sample

The government distribution channels of medicines uses the 'Vital Essential Necessary' system whereby the public institutions are divided into referral health institutions and primary health care centres (National Medicines and Therapeutics Advisory Committee, 2015). The primary health institutions are for management of minor ailments and chronic conditions routine monitoring, whilst they refer to the referral hospitals. All the hospital were considered for the study because of their small number. These were:

(i) Chitungwiza General Hospital
(ii) Harare Central Hospital
(iii) Parirenyatwa Group of Hospitals

The Medicines Control Authority of Zimbabwe had 250 pharmacies licensed in the area of interest at the time of the study.

1.5.1.3 Sample Size

A statistical software was used to calculate the sample size of the pharmacies and the public health institutions. The sample size calculator is found on www.surveysystem.com/sscalc.htm#two

Sample size for the private pharmacies

Confidence level 95%

Confidence Interval 5

Population 250

Sample size 150

Sample size for the public institutions

Confidence level 95%

Confidence Interval 5

Population 3

Sample size 3

1.5.1.4 Sampling

Multi-stage random sampling was used to sample 150 of the 250 pharmacies in the areas of interest. The Medicines Control Authority of Zimbabwe's premises database was used for sampling purposes (MCAZ, 2018). All the licensed pharmacies in Harare were extracted from the database and then stratified into those from high density areas and those from low density areas. A systematic random sampling approach was then used on the strata were those even number pharmacies on the strata were chosen. Convenience sampling was used on the government's referral hospitals. Stratification ensured that the health institutions were as representative of the population as is possible and eliminate the location bias. Convenience sampling has the advantages of being cheap and in most instances more feasible to the setting (Black, 1999).

1.5.1.5 Recruitment approval process.

Letters were written to seek approval from the following departments:

(i) Director Health Services Chitungwiza for the Municipality owned institutions.
(ii) Clinical Directors Harare, Parirenyatwa and Harare Hospitals.
(iii) For the pharmacies, authorisation was sort from each facility's directors before study could be conducted.

1.5.1.6 Inclusion criteria for the antineoplastic medicines

- Antineoplastic medicines that have been issued a registration certificate in Zimbabwe.
- Antineoplastic medicines that have been imported into the country through the 'section 75' process in the year 2018.

1.5.1.7 Exclusion criteria for the antineoplastic medicines

- Antineoplastic medicines that have been registered and are on the MCAZ drug register but have not been imported into the country in the past year.

1.5.1.8 Data Collection Tool/Methodology

A data collection form-based cross sectional survey was conducted in public and private medicine outlets. A pre-structured data collection form was used (WHO, 2005). The data form was administered by the investigator as a hard copy in 3 (three) public institutions and 150 private health institutions in Harare and Chitungwiza from July to September 2018. The pharmacy supervisors provided the data from their dispensing software and records. This data was inclusive of the dispensing fees.

The survey tool focused on the following areas:

- Type of institution from which data was collected.
- Medicine generic name, dosage form, strength.
- Manufacturer.
- Availability at the institution.
- Price of the medicine (Procurement price).
- Selling price of the medicine.
- Mark-ups of the medicine (Selling price - Aquisition price).

- Affordability (Calculated as the number of days' wage of the least paid government worker which was pegged at USD296 (Zimbabwe National Statistics Agency, 2018). The affordability of the medicines was calculated based on the medicine required for a month's treatment of various type of cancers as stipulated in the British National Formulary and the digital prescribers' registry (Prescribers Registry, 2018).

1.5.2 Data Analysis

Availability

A ratio scale variable, availability, was calculated as the number of institutions that had the medicine on the day of the study as a percentage of the total number of institutions that were visited. Availability in the public institutions was compared against availability in private institutions. Descriptive measures like percentages and means were calculated.

Affordability

Affordability was calculated from the minimum government wage/salary of USD 296. The days' wages were calculated using the unit antineoplastic price i.e the price of unit tablet or vial. The monthly or cycle amount of an antineoplastic medicine was considered using the standard prescribing doses for the medicines i.e $296 divided by 30 days = 9.86 day wage. This then was then used to calculate the number of wage days to acquire the antineoplastic medicine (Alefan, 2018).

Average cost price

A ratio scale variable, average cost price of the medicine was calculated by finding the average sample price for a medicine on those institution that had the medicine on the date of survey expressed in USD. Descriptive statistics range, median, mode and mean were calculated.

Median price ratio

A ratio scale variable median price ratio was calculated for all the medicines using the following equation:

$$\frac{median\ local\ unit\ price}{international\ reference\ unit\ price}$$

The WHO International Medical Price list was used for the international reference unit price (WHO/Management Science Health, 2015). Median price ratios were calculated for twenty (22) of the twenty nine (29) medicines that had been sampled in the population. The inclusion criteria for these medicines was an availability of an international reference unit price in WHO's reference unit price list.

Table 4: List of medicines and their international reference price

Product Description	International Reference Price in USD	Price per unit
Letrozole 2.5mg tablets	0.4179	price per tablet
Rituximab 100mg injection	13.6721	price/ml
Tamoxifen 20mg tablets	0.1243	price per tablet
Oxaliplatin 50mg injection	28.8821	price per vial
Oxaliplatin 100mg injection	74.7676	price per vial
Paclitaxel 100mg injection	11.048	price per vial
Paclitaxel 30mg injection	0.8754	price per ml
Carboplatin 450mg injection	40.3245	price per vial
Carboplatin 150mg injection	16.0053	price per vial
Cisplatin 0.5mg injection	0.515	price per ml
Vincristine 1mg/ml injection	2.5416	price per vial
Vinblastine 10mg/10ml injection	4.9762	price per vial
Vinorelbin 10mg/ml injection	21.965	price per vial
Imatinib 400mg tablets	25.2098	price per tablet
Methotrexate 2.5mg tablets	0.1573	price per tablet
Methotrexate25mg/5ml injection	2.6258	price per vial
Fluoro-uracil 50mg injection	0.2048	price per ml
Anastrazole 1mg tablets	0.5271	price per tablet
Bicalutamide 50mg tablets	0.2343	price per tablet
Doxorubicin 50mg injection	5.4059	price per vial
cyclophosphamide 500mg injection	8.16	price per vial
Docetaxel 80mg injection	17.514	price per vial

Price mark-ups

An average mark-up per facility was calculated and then an average sample mark-up price was calculated. Descriptive statistics that were calculated included the mean, mode and median mark-ups.

Study sample

A total of one hundred and sixty (160) data sheets were distributed in private pharmacies, of these one hundred and fifty (150) pharmacies responded. Statistical inferences were made from these.

This data was transcribed to Microsoft Excel ®. Statistical analysis such as measures of central tendency and measure of dispersion were calculated from this data.

1.5.2.1 Statistical Analysis

The data was subsequently exported to and analysed using International Business Machines (IBM)'s Statistical Package of the Social Sciences (SPSS) ®, version 23.

1.5.2.2 Data Cleaning

For accuracy of transcription, a second person checked the numerical entries for every data sheet to verify the correctness of the data.

1.5.2.3 Data Management

To protect the identity of the pharmacy respondents and to eliminate bias, pharmacy codes were used. The data sheets were stored on a password protected computer and backed-up on a password protected hard drive and a copy was stored on the Google drive ®.

1.5.2.4 Pilot Study

The data collection tool was validated by a pilot study that involved 15 pharmacies. The number was calculated as 10% of the proposed samples. Convenience sampling was used for the pilot study sample.

1.5.2.5 Ethical Approval

Ethical approval for the study was obtained from the Biomedical Research Ethics Committee of the University of KwaZulu-Natal (BE 644/17) - (Annexure 1), as well as from the Medical and Research Council of Zimbabwe (MRCZ/B/1524) - (Annexure 2).

1.6 Conclusions

The introductory chapter looked at the current situation of the problem in Zimbabwe. It also explained the micro and macro-economic issues surrounding the health sector. The chapter identified the policy issues in Zimbabwe. The chapter introduced the key concepts of the study which are accessibility, availability and affordability of antineoplastic medicines. The chapter looked at the significance of the study, the research aims and objectives and explored the general methodology of the study.

CHAPTER 2

LITERATURE REVIEW

2.1 Introduction

The previous chapter was an introduction to the area of study. This chapter explores the information available in the literature for the researcher to get an understanding of the price, availability and affordability of antineoplastic medicines from a theoretical perspective. This chapter additionally looks at the WHO/HAI method and explores studies done in resource limited settings to see the price, availability and the affordability of antineoplastic medicines.

2.1.2 Cross sectional surveys

Cross sectional studies measure the prevalence of health outcomes or determinants of health in a population at a point in time. For success and credibility of the study there is a need for early planning. This is achieved by being able to translate the interest of the study to precisely formulated study objectives, choosing the correct sample size, suitable sampling methods, response rates and effective parameter analysis (Coggon D et al., 2003).

The study used a cross sectional study approach (Sedgwick, 2014). This has a number of advantages, as follows:

(i) Ability to rapidly generate data and infer on some health related events for policy makers or for generating hypotheses on the topic or for further research.

(ii) Cross sectional studies are easy to conduct and affordable as compared to other forms of research where there is need of follow-up of participants.

(iii) There is good control of the variable under study because of the one point measurement approach.

(iv) It offers complete data as all variables are measured and data collected at once.

(v) Data collected by cross sectional studies can be used for additional secondary analysis.

(vi) It allows researchers to study multiple outcomes and exposures at once.

(vii) There is no loss to follow up as data is collected as participants are interviewed only once.

(viii) With the advent of new technology analysis of cross sectional survey data is easy and descriptive statistical parameters can be easily calculated.

Cross sectional studies have a number of disadvantages:

(i) Study is ineffective if it is non-representative of the entire population.
(ii) It requires a large sample for the data to be correct.
(iii) Non responsiveness can result in bias of results.
(iv) It is often associated with the temporal confusion bias called Protopathic bias.
(v) It does not establish causal relationship between variables.
(vi) Most surveys lacks desired number of participants for study to be statistically significant. In some instances it is inevitable to realise that the participants' numbers does not even permit the achievement of the study's primary objective. Also non responders to a survey maybe atypical representing a subgroup of the population with vital inferences to the study (Coggon D et al., 2003).

2.1.1 Price and availability surveys

Many surveys have been done to assess the price and availability of medicines in different jurisdictions using cross sectional surveys. These surveys collected both qualitative and quantitative data that has been used to for policy formulation and implantation. Such studies included the study by Marume, 2015, Mhlanga and Suleman, 2014 and Maponga et al., 2009. These and many studies were based on the WHO/HAI medicines survey approach. This is a self-administered questionnaire based study with an advantage of response standardisation (Coggon D et al., 2003).

2.1.2 The WHO/HAI Project

The WHO/HAI Project on medicine prices and availability was adopted for this study. This is a project that was developed after it was noted that there was a need for increased access to medicines as part of the fight against poverty (WHO/HAI, 2008). Also there were few studies that had been done in developing countries to measure medicine prices and make international comparisons. The absence of a standard methodology to assess medicine availability and affordability was seen as a stumbling block. In 2001 the WHO/HAI Project in medicines prices and availability was introduced. The main objective was to develop a reliable methodology for collecting and analysing medicine price, availability and affordability data. By the end of 2007, over 50 surveys had been undertaken worldwide (WHO/HAI, 2008). The results of these studies are as below:

(i) Medicine prices are high, especially in the private sector (up to 80 times the International Reference Price) (WHO/HAI, 2008).

(ii) Availability was particularly low in the public sector (WHO/HAI, 2008).

(iii) Treatment was often unaffordable e.g. requiring over 15 days' wage to purchase (WHO/HAI, 2008).

(iv) Mark-ups in the distribution chain were excessive (WHO/HAI, 2008).

(v) Numerous taxes and duties were being applied to medicines (WHO/HAI, 2008).

2.1.3 Medicine price, availability and affordability studies

Maponga, et al., conducted a cross sectional study entitled, 'The price people pay for medicines in Zimbabwe' (Maponga et al., 2009). The study concluded that medicine prices in Zimbabwe were high. A scenario that would compromise affordability and accessibility to medicines especially by the poor. Urgent steps were needed to reduce the level and effect of the high prices on the population, especially the poor. The study revealed that innovator brands in the private sector were priced 10 times the International References Prices (IRP) and more than three times the price of generic medicines.

Mendis conducted a study on the availability and affordability of selected essential medicines for chronic diseases in six low-and-middle income countries (Mendis, 2007). He conducted a survey of the availability and price of thirty two (32) medicines in a representative sample of public and private medicine outlets in four geographical areas. He found out that generally total availability of medicines in the public sector was considerably lower in all the countries. From the research he concluded that context specific policies were required to improve access to essential medicines. He also recommended that prices could be reduced by improving purchasing efficiency, eliminating taxes and regulating mark-ups (Mendis, 2007). These are important recommendations especially the mark-up regulations, as currently in Zimbabwe there is no regulation of mark-ups on medicines.

A study was conducted by (Sado and Sufa, 2016) on availability and affordability of essential medicines for children in the western part of Ethiopia using the WHO and HAI tools to measure availability, affordability, and prices of essential medicines. They expressed availability as a percentage of drug outlets per sector that stocked surveyed medicines on the date of data collection. From the study, percentage availability of essential medicines in the public sector was 4% and 42.8% in private sector. Lowest priced medicines were sold at 1.18 and 1.54 times their International Reference Prices in the public and private sectors respectively. Medicines

were unaffordable as they costed a day or more day's wages for the lowest paid government unskilled worker. They concluded that further studies on a large scale were critical to identify acute areas for policy interventions such as price and or supply (Sado and Sufa , 2016).

A study in Delhi entitled, 'Where are we now: assessing the price, availability and affordability of essential medicines in Delhi as India plans for free medicines for all' by Kotwani was conducted under the background that inequitable access to medicines was a major weakness in the Indian health care system. Baseline data was needed to develop effective public health policy and provide equitable access to essential medicines using the standardised WHO/HAI methodology. Data on price and availability of medicines was collected from private retail and chain pharmacies of a leading corporate house. Prices were compared to an international reference price (expressed as median price ratio-MPR). The results of the study indicated that the procurement price of surveyed medicines were 0.53-0.82 times the IRP. The overall mean availability of surveyed medicines in public facilities was 41.4%. From their study it was evident that the majority of India's population could not afford the prices of the essential medicines. They concluded that the availability was very poor in public sector facilities and was better in private retail pharmacies but affordability remained a big challenge for a majority of the population (Kotwani, 2013).

A study was conducted by (Babar et al., 2007) in Malaysia entitled, Affordability, and Price components: Implications for Access to Drugs in Malaysia, in a background that the health care system was facing challenges with increasing medicine costs. The study was conducted to evaluate the medicines prices, availability, affordability and the structure of price components. The study was conducted in 20 public hospitals, 32 private sector pharmacies and 20 dispensing doctors' clinics. Medicine prices were compared with IRPs. In private pharmacies, innovator brands (IB) were 16 times higher than the IRPs. They concluded that in the private sector there was a very low median availability of 25%. A low availability of medicines on the National Essential Drug list and the drug formulary were found in all sectors. This is the issue with anticancer medicines here in Zimbabwe. Also on the price components, add-on costs had a substantial impact on medicine prices.

A study by Mhlanga and Suleman in Swaziland determined the prices, availability and affordability of medicines along the supply chain. They used the WHO/HAI standardised methodology. From the study the mean availability of essential medicines was 68% in the public sector. The total cumulative mark-ups for individual medicines ranged from 190.99%-

440.27%. The largest contributor to add-on cost was the retail mark-up which ranged from 31-53%. From the study they concluded that policy measures such as price capping could increase availability of drugs. This could be the case with the Zimbabwean system where there is no price control.

A study conducted by Yohana on the availability and affordability of anticancer medicines in Dar Es Salaam, Tanzania, in the background where there was little documented information regarding the availability and affordability of antineoplastic medicines at the patient level. From the cross sectional study conducted on outpatients attending the ORCI clinic, they concluded that the availability of antineoplastic medicines was inadequate. Also the prices of the medicines in the private pharmacies were high and most of the patients were not on medical aid (Yohana, 2010).

According to a paper on Millennium Development Goals (WHO, 2014) , several countries have made substantial progress towards increasing access to essential medicines, but access to essential medicines is still not adequate in developing countries. According to the paper, the availability of medicines in the public sector, was only one third whilst in the private sector was two thirds and the prices that people paid for the lowest priced generic medicines varied from 2.5 times to 6.5 times International Reference Prices in the public and private sectors respectively. The millennium development goal target 8.E, which states that in cooperation with pharmaceutical companies, governments should be able to provide access to affordable essential drugs in developing countries. The proposed indicator was the proportion of the population with access to affordable essential medicines on a sustainable basis. In the 27 countries in which data was available, average public sector availability of essential drugs was 34.9%. The paper also indicated that low availability of medicines in the public sector could be attributed to insufficient funds. The paper also indicated that even though the national government procurement prices are usually close to or below the international prices, patients paid more owing to mark-ups in the supply chain (WHO, 2014).

Taxes and duties were identified as other contributors to add-on costs in the supply chain. They proposed that medicine prices could be reduced by eliminating duties and taxes on medicines. This already is the case here in Zimbabwe, were importers of antineoplastic medicines get tax exemption when they apply for it through the Ministry of Health. However, even though there is this tax exemption, there is a likelihood that the medicines are still being sold at prices that are above the International Reference Prices (WHO, 2014).

According to the Global Health Observatory (GHO) data, in low and middle income countries, prices of selected lowest priced generics can be more than twice IRPs. Cases in point were Congo, Phillipines and Moldova public sectors were patient prices in the public sector were over 400% higher than the International Reference Prices. In the private sector the price of generics ranged from 32% to 2700% of the International Reference Price (WHO, 2018).

2.1.3 International reference price and median price ratios

Medicine prices are expressed as ratios relative to a standard set of reference prices. These are listed in the International Medicines Price Indicator guide (WHO/ Management Science Health, 2015). Median price ratio is calculated for medicines using the following equation:

$$\frac{median\ local\ unit\ price}{international\ reference\ unit\ price}$$

Median price ratios have been used in studies to compare the price of medicines in specific jurisdictions to international prices. Jason Shaffrin stated that, IRP is a system whereby a country states that they will pay no more than the price paid by another country or a basket of countries. In theory, countries could also regulate drug prices by saying that they would not pay more than X% of country A's price or X% of the reference basket of country A, B and C (Shaffrin J, 2015).

2.1.4 Antineoplastic medicines registration, accessibility and oncology care in Zimbabwe

According to the publication by the Zimbabwe National Cancer Registry, the total incidences of new cancer cases recorded in Zimbabwe in 2015 was 7 165, comprising 3 041 (42.4%) males and 4 124 (57.6%) females. In Harare City a total of 2 518 malignant tumors were registered in 2015. These comprised 1 179 (46.8%) males and 1 339 (53.2%) females (Zimbabwe National Cancer Registry, 2015).

The most frequently occurring cancers among Zimbabweans of all races in 2015 were cervix uteri (19%), prostate (9%), breast (7%), Kaposi sarcoma (KS) (7%), non-melanoma skin cancer (NMSC) (6%), non-Hodgkin lymphoma (NHL) (6%), esophagus (5%), colo-rectal (4%) and stomach (3%). The other cancers accounted for 34% of the registered cancers (Zimbabwe National Cancer Registry, 2015).

There are no antineoplastic medicines readily manufactured in Zimbabwe. Zimbabwe depends on importation of finished pharmaceutical products from India and Europe (MCAZ, 2018).

According to the Ministry of Health and Childcare, only one public facility in Harare, Parirenyatwa Hospital provides oncology care. Patients also heavily rely on the private sector for access to antineoplastic medicines.

2.1.5 Areas of agreement of background studies

Most of the studies that were incorporated into the literature review used the WHO/HAI methodology. The main objectives in the studies sought to determine the accessibility and availability of essential medicines.

Most of the studies agreed that the essential medicines were unavailable in the public sector and also that the medicines were highly priced in most of the private pharmacies.

Most of the studies concluded that there was a need of policy changes to ensure that there was some form of price regulation and policies that favours availability of medicines to the general public.

2.1.6 Areas of disagreement of background studies

The study in Sri Lanka was the only one that showed, that essential medicines were fairly available in public institutions (Dabare *et al*, 2014)

2.1.7 Recommendations from reviewed studies

The paper on the millennium development goals, recommended that there was need for further support for chronic, non-communicable diseases such as cancer. They recommended that tax and duty reduction or exemptions on medicines were pivotal in the increase of access to essential medicines (WHO, 2014).

It was also recommended that generally there was a need to use quality assured generic medicines that tend to be cheaper than the brand innovators. The National Cancer Prevention and Control Strategy in Zimbabwe, said there was a need to have research in priority areas such as determining effective ways to improve access to quality cancer health care services to decrease the health care costs associated with cancer prevention and cancer treatment. Also there was a need to ascertain the feasibility of introducing a cancer levy (ZIMSTATS, 2018).

The study by Mendis et al., recommended that there was a need for policies that address a country's circumstances to improve accessibility of essential medicines. They also suggested that pooling procurement can be an effective policy to improve purchasing efficiency, eliminating taxes, regulating mark-up and monitoring the supply chain. Should need arise,

sometimes there is need to regulate prices through the enforcement of maximum mark-up and maximum selling prices (Mendis et al., 2007).

CHAPTER 3 FINDINGS

3.1 Introduction

This chapter presents the findings from the study and interprets them through a discursive section. Conclusions are then made from the interpretations.

3.2 Findings

3.2.1 Availability of antineoplastic medicines in private Sector

Availability was presented as very poorly available i,e ≤10% availability in the institutions that were surveyed, poorly available that is 10.1%-20.9% availability in the institutions that were surveyed, fairly available 21%-29.9% availability in the institutions surveyed and better available 30-50% availability in the institutions surveyed. This presentation of availability was adapted from availability presentation from a study by Alefan et al., 2018.

Table 5: Availability of antineoplastic medicine in the private sector

Antineoplastic medicine	Availability N=150	Percentage Availability	Availability
Bleomycin 15 IU injection	0	0	very poorly available ≤10%
Darcabazine 200mg injection	0	0	
Imatinib 400mg tablets	1	1%	
Sorafenib 200mg tablets	2	1.3%	
Docetaxel 80mg injection	2	1.3%	
Rituximab 100mg injection	4	2.7%	
Doxorubicin 50mg injection	4	2.7%	
Methotrexate 25mg/5ml injection	6	4%	
Paclitaxel 30mg injection	6	4%	
Aberaterone 250mg tablets	6	4%	
Cyclophosphamide 500mg injection	6	4%	
Carboplatin 450mg injection	8	5.3%	
Vinorelbin 10mg/ml injection	8	5.3%	
Paclitaxel 100mg injection	8	5.3%	
Rituximab 11.7mg/injection	10	7%	
Paclitaxel 300mg injection	12	8%	
Oxaliplatin 50mg injection	12	8%	
Cisplatin 0.5mg injection	14	9.3%	
Oxaliplatin 100mg injection	22	9.8%	
Bevacizumab 25mg injection	16	10.7%	poorly available 10.1%-20.9%
Trastuzumab 440mg injection	16	10.7%	
Vinblastine 10mg/10ml injection	16	10.7%	
Carboplatin 150mg injection	20	13.3%	

Fluoro-uracil 50mg injection	20	13.3%	
Vincristine 1mg/ml injection	30	20%	
Anastrazole 1mg tablets	30	20%	
Letrozole 2.5mg tablets per 30	32	21%	fairly available 21%-29.9%
Goserelin 3.6mg injection	34	26.7%	
Tamoxifen 20mg per 30 tablets	40	26.7%	
Goserelin 10.8mg injection	44	29.3%	
Bicalutamide 50mg tablets	48	32%	better available 30-50%
Methotrexate 2.5mg tablets	64	42.7	

Nineteen (19) of the thirty two (32) medicines were very poorly available in private sector with an availability of less than 10%. Seven (7) of the thirty two (32) medicines were poorly available with an availability of greater than 10% but less than 21%. Four (4) of the thirty two (32) medicines had a fairly available status. Two (2) of the thirty two (32) medicines namely Bicalutamide 50mg tablets and Methotrexate 2.5mg tablets had better availability of between 30% and 50%. Average percentage availability was 12.38% for the sampled medicines in Harare's private pharmacies.

3.1.2 Availability in public sector

Table 6: Availability of antineoplastic medicine in the public sector

Antineoplastic medicine	Availability N=1	Availability
Methotrexate 25mg/5ml injection	Yes	Available
Cyclophosphamide 200mg injection	Yes	
Doxorubicin 50mg injection	Yes	
Carboplatin 450mg injection	Yes	
Paclitaxel 300mg injection	Yes	
Vincristine 1mg/ml injection	Yes	
Bleomycin 15 IU injection	Yes	
Darcabazine 200mg injection	Yes	
Docetaxel 80mg injection	No	Unavailable
Rituximab 100mg injection	No	
Imatinib 400mg tablets	No	
Methotrexate 2.5mg tablets	No	
Paclitaxel 30mg injection	No	
Aberaterone 250mg tablets	No	
Vinorelbin 10mg/ml injection	No	
Paclitaxel 100mg injection	No	
Rituximab 11.7mg/injection	No	

Oxaliplatin 50mg injection	No	
Cisplatin 0.5mg injection	No	
Oxaliplatin 100mg injection	No	
Bevacizumab 25mg injection	No	
Sorafenib 200mg tablets	No	
Trastuzumab 440mg injection	No	
Vinblastine 10mg/10ml injection	No	
Carboplatin 150mg injection	No	
Fluoro-uracil 50mg injection	No	
Anastrazole 1mg tablets	No	
Letrozole 2.5mg tablets	No	
Goserelin 3.6mg injection	No	
Tamoxifen 20mg tablets	No	
Goserelin 10.8mg injection	No	
Bicalutamide 50mg tablets	No	

At Parirenyatwa hospital eight (8) of the thirty two (32) surveyed medicines were available. This represented a total of 25% medicines availability.

3.2.3 Median price ratio for the private sector pharmacies

Table 4 shows the median price ratio for private sector pharmacies

Table 7: Median price ratio for the private sector pharmacies

Product Description	International reference price in USD	Local median price in USD	Median price ratio
Cisplatin 0.5mg injection	0.515 price per ml	0.315 price per ml	0.6
Oxaliplatin 100mg injection	74.7676 price per vial	64.5 per vial	0.86
Vinblastine 10mg/10ml injection	4.9762 price per vial	5 per vial	1
cyclophosphamide 500mg injection	8.16 price per vial	9 price per vial	1.10
Methotrexate 2.5mg tablets	0.1573 price per tablet	0.18 per tablet	1.14
Rituximab 100mg injection	13.6721 price/ml	18 price/ml	1.30
Imatinib 400mg tablets	25.2098 price per tablet	35 price per tablet	1.38
Oxaliplatin 50mg injection	28.8821 price per vial	41 per vial	1.42
Vincristine 1mg/ml injection	2.5416 price per vial	4.50 price per vial	1.77
Carboplatin 450mg injection	40.3245 price per vial	81.10 per vial	2
Methotrexate25mg/5ml injection	2.6258 price per vial	5.78 per vial	2.20
Fluoro-uracil 50mg injection	0.2048 price per ml	0.6 per ml	3
letrozole 2.5mg tablets	0.4179 price per tablet	1.42 price per tablet	3.2
Doxorubicin 50mg injection	5.4059 price per vial	23 price per vial	4.2
Paclitaxel 30mg injection	0.8754 price per ml	3.7 per ml	4.22
Carboplatin 150mg injection	16.0053 price per vial	69.5 per vial	4.34
Paclitaxel 100mg injection	11.048 price per vial	60 per vial	6

Anastrazole 1mg tablets	0.5271 price per tablet	3.56 per tablet	6.7
Bicalutamide 50mg tablets	0.2343 price per tab	1.7 per tablet	7
Docetaxel 80mg injection	17.514 price per vial	135 price per vial	7.9
Vinorelbin 10mg/ml	21.965 price per vial	220 price per vial	10
Tamoxifen 20mg tablets	0.1243 price per tablet	1.37 per tablet	11

Median price ratios were calculated for twenty-two (22) of the medicines. These medicines were included on the basis of having an IRP in the WHO's International Medicines Guide of 2015. Fifty percent of the antineoplastic medicines had a price ratio of lower than 4 in the private sector. Only two medicines, Tamoxifen 20mg tablets and Vinorelbin 10mg/ml injection had MPRs greater than 10 in the private sector. The MPRs for the medicines in private sector ranged from 0.60 to 11.

3.2.4 Median Price Ratio for the public sector pharmacies

Table 5 shows the median price ratio for public sector pharmacies.

Table 8: Median price ratio for the public sector pharmacies

Product Description	International Reference Price in USD	Local hospital median price in USD	Median price ratio
Paclitaxel 300mg/50ml injection	0.8754 per ml	0.636 per ml	0.73
Cyclophosphamide 200mg injection	4.2070 price per vial	3.80 price per vial	0.90
Doxorubicin 50mg injection	5.4059 price per vial	5.99 price per vial	1.11
Carboplatin 450mg injection	40.3245 price per vial	47.50 per vial	1.18
Vincristine 1mg/ml injection	2.5416 price per vial	3.00 per vial	1.18
Bleomycin 15U injection	12.3210 price per vial	25.70 per vial	2.09
Methotrexate25mg/5ml injection	2.6258 price per vial	5.90 per vial	2.25

Median price ratios were calculated for seven (7) of the medicines that were available in the public sector. These medicines were included on the basis of having an IRP in the WHO's International Medicines Guide of 2015. Two (2) of the antineoplastic medicines, Paclitaxel injection and Cyclophosphamide injection had price ratios of lower than 1 in the public sector, meaning they were being sold lower than the IRP. The MPR for the antineoplastic medicines ranged from 0.73 to 2.25.

3.2.5 Affordability

Affordability was calculated from the minimum government wage/salary of USD 296. The days' wages were calculated using the unit antineoplastic price i.e the price of unit tablet or

vial. (WHO, 2018). The monthly or cycle amount of an antineoplastic medicine was considered using the standard prescribing doses for the medicines i.e $296 divided by 30 days = 9.86 day wage. This then was used to calculate the number of wage days to acquire the antineoplastic medicine (Alefan, 2018).

Table 6 shows affordability in the private sector

Table 9: Affordability in private sector

Antineoplastic medicine	Median Cost Price in USD	Cost for one Month supply in USD	Days wages Wage	Affordability
Cyclophosphamide 500mg injection	9	9	1 day	Affordable
Vincristine 1mg/ml injection	4.50	4.50	1 day	
Sorafenib 200mg tablets	520	35	4 days	
Methotrexate 2.5mg tablets	18	36	4 days	
Tamoxifen 20mg tablets	41	41.00	5 days	
Letrozole 2.5mg tablets	42.5	42.50	5 days	
Vinblastine 10mg/10ml injection	50	50	5 days	
Methotrexate25mg/5ml injection	5.78	50	5 days	
Bicalutamide 50mg tablets	51	51	6 days	
Paclitaxel 300mg injection	69.5	69.50	7 days	
Bevacizumab 25mg injection	94	94	10 days	
Fluoro-uracil 50mg injection	6	108	11 days	Slightly affordable
Anastrazole 1mg tablets	107	107	11 days	
Oxaliplatin 50mg injection	41	123	13 days	
Doxorubicin 50mg injection	23	125	13 days	
Oxaliplatin 100mg injection	64.5	129	13 days	
Cisplatin 0.5mg injection	15.75	157.50	16 days	
Carboplatin 450mg injection	81.10	162.20	17 days	
Paclitaxel 100mg injection	60	190	20 days	
Goserelin 3.6mg injection	203	203	21 days	Unaffordable
Carboplatin 150mg injection	69.5	251.6	26 days	
Goserelin 10.8mg injection	403	403	41 days	
Docetaxel 80mg injection	135	405	41 days	
Vinorelbin 10mg/ml injection	220	440	45 days	
Rituximab 100mg injection	980	980	100 days	Highly Unaffordable
Abiraterone 250mg tablets	1040	1040	106 days	
Imatinib 400mg tablets	1050	1050	106 days	
Rituximab 1400mg/11.7ml injection	1806	1806	184 days	
Trastuzumab 440mg injection	2422	4822	490 days	

Eleven (11) of the medicines in the private sector were affordable with ten (10) wage days and below. Eight (8) of the medicines were slightly affordable with wage days more than 10 days but less than twenty (20) days. Five (5) of the medicines had wage days more than twenty (20) days. Five (5) of the medicines were highly unaffordable with days' wages of more than 100 days to 490 days. From the results the medicines were generally unaffordable on the patient part.

3.2.6 Affordability in the public sector

Table 7 shows affordability in the public sector.

Table 10: Affordability in public sector

Antineoplastic medicine	Median Cost Price in USD	Cost for one Month supply in USD	Days wages Wage of 296 9.86 per day	Affordability
Vincristine 1mg/ml injection	3.00	3.00	1 day	Very Affordable
Cyclophosphamide 200mg injection	3.80	68.40	1 day	
Doxorubicin 50mg injection	5.99	45.32	5 days	
Methotrexate25mg/5ml injection	5.90	47.20	5 days	
Bleomycin 15U injection	25.70	77.10	8 days	
Carboplatin 450mg injection	47.50	95.00	10 days	
Paclitaxel 300mg/50ml injection	31.80	95.40	10 days	

Generally antineoplastic medicines were affordable in the public sector as compared to the private sector. All the medicines were within 10 days wage. However of the 29 medicines that were considered for the study, only seven medicines were available. This means that regardless of the low prices at public institutions, the out-of-pocket fees by the patients were still considerably high as there was a need to source all the unavailable medicines in the public sector.

3.2.7 Percentage Mark Up

Average Mark-up in Private Sector	Average Mark-up in Public Sector
51.3%	34.0%

The average percentage mark-up in the private sector was 51.3% and the range was 45% to 73%. This was derived by calculating the average mark-up, which was the difference in cost price of a medicine and the selling price of the medicines found at a facility and then the total

average for the private. The average mark-up at the private sector was 34% and the range for the mark-up was 2% to 64%.

CHAPTER 4 DISCUSSION

4.1 Discussion

Introduction

This chapter analyses the results and makes statistical inferences from them. It discusses the availability in private and public sector, median price ratio, affordability of antineoplastic medicines and percentage mark-ups

4.1 Availability in the private and public sector

Medicines were generally more available in the private sector. Thirty (30) of the thirty two (32) medicines were available in the private sector pharmacies. This was a percentage availability of 98%. Availability was very low in the public sector. Only eight (8) of the thirty two (32) medicines were available. This was a percentage availability of 25%. This finding was the same with the findings of a study by Kotwani, et al. where the mean availability of essential medicines in Dehli was 41.3% in facilities that were under the government control. According to the study by Kotwani et al., medicines availability was better in the private retail pharmacies as compared to the public facilities. Also the dedication of two hospitals for cancer treatment in the whole country had an implication on accessibility of consultation services and chemotherapy services. The results also compared with the study by Babar et al. on the study entitled, 'Affordability, and price components: implication to access in Malaysia'. The results of the study showed that there was 25% availability of medicines in the public sector and the median availability was higher in private institutions at 45%. Unavailability of medicines in the public sector in Zimbabwe show a different picture with the other studies that were done previously by other researchers. In 2016 in their study on essential medicines, Marume and Bangalee, 2016 had essential medicines availability of greater than 80%. This shows a decline in availability from previous years in the public sector. However it should be noted that the studies mentioned focused on all essential medicines, none focused on antineoplastic medicines only.

The findings in the current study makes it evident that there is spiral decline in availability and hence implications on access of antineoplastic medicines and all essential medicines in general.

4.2 Median price ratio

The median price ratios in private pharmacies of 0.6 to 11 were calculated in the study, for the 22 medicines. Medicines price as considerably high in the private sector compared to the public

sector which had a median price ratio which ranged from 0.73 to 2.25. The medicines which had high median price ratios were those patented products that did not have cheaper alternative generics. This means antineoplastic medicines were sold 0.6 to 11 times higher in the private retail pharmacies compared to the International Reference Prices.

Studies done by previous researchers on price and availability of general medicines in Zimbabwe, had an average MRP of 1.5 in public sector compared to the 0.73 to 2.25 in the current study (Marume and Bangalee, 2016). The MRP of this current study of 0.60 to 11 resonated with the finding of the Marume and Bangalee study where they had an MRP of 10 for medicines in the private sector. This high MRP and low affordability has an implication on access of antineoplastic medicines.

4.3 Affordability

Generally antineoplastic medicines were affordable in the public sector as compared to the private sector. All the medicines were within ten (10) days' wage compared with the days' wages for private retail pharmacies which ranged from 1 day to 490 days. However of the 32 medicines that were considered for the study, only nine medicines were available in public institutions. This therefore means the more expensive and highly unaffordable medicines that were not available might have contributed to the low days' wages. For those same medicines that were available at both the public and private institutions, the differences were very minimal. Cases in point were those of methotrexate 25mg/5ml injection which had a median price ratio of 5.90 for public institutions and 5.78 for private institutions. There was no significant difference between the MRP. The results shows that regardless of the low prices at public institutions, the out - of - pocket fees by the patients were still considerably high, as there was still a need to source for medicines they can't access in the public sector. The finding of the study was in-line with the technical report on pricing of cancer medicines (WHO, 2019). They reported that there has been an in increase in the spending on cancer medicines from US$90.9 billion in 2012 to US$133 in 2017. They reported that per capita spending on cancer medicines has increased by 2 to 8 fold the overall per capita on health expenditure.

Eleven (11) of the medicines in the private sector were affordable with ten (10) wage days and below. Eight (8) of the medicines were slightly affordable with wage days more than ten (10) days but less than 20 days. Five (5) of the medicines had wage days more than 20 days. Five (5) of the medicines were highly unaffordable with days wages of more than 100 days to 490 days. From the results the medicines were generally unaffordable on the patient part. The

findings of the study was contrary to with the findings of Alefan et al., 2018 in which their study in Jordan revealed that more of the essential medicines were affordable costing up to 1 days wage or less.

4.4 Percentage mark-up

The average percentage mark-up in the private sector was 51.3% and the range was 45% to 73%, whilst the average mark-up at the private sector was 34% and the range for the mark-up was 2% to 64%. The difference in prices is explained by the differences in the operational costs.

Government needs to capacitate local industry on antineoplastic medicines dossier acquisition and manufacturing industry resuscitation so that products are manufactured locally. This reduces transport costs which also imparts on the overall price of medicines. This also increases competition and hence has the potential to reduce prices and the price burden on the patients.

4.5 Study strength

- The study used a worldwide WHO/HAI recognised study methodology (WHO/HAI, 2008).
- The study sample was calculated using a 95% confidence level and a 5% confidence interval. This means the sample is a good representation of the population.
- The study used stratification and random sampling for the samples which eliminates bias (Black, 1999).

4.6 Limitations of the study

- There are no major studies that have been done in Zimbabwe and the region on the price and availability of antineoplastic medicines, hence background information was very limited.
- There was low medicines availability in public sector which compromised the median price ratio comparison between the private and public sector.
- Also affordability was calculated on the wage/salary of the least paid government worker, this is not indicative enough in an economic environment with a greater than 60% unemployment rate. It is difficult to translate the affordability to the generally unemployed population (ZIMSTATS, 2018).

- Not all antineoplastic medicines had IRPs. This resulted in other medicines not being considered for MPRs and hence limited the quality of data.

CHAPTER 5 CONCLUSION

The generic medicines policy should be used as the median prices of generic medicines tend to be low as compared to the brand medicines. The MRPs of antineoplastic medicines in Zimbabwe for both the private and public institutions have shown that the medicines are not highly priced compared to the IRP taking into consideration the fact that we are not manufacturing any of the antineoplastic medicines.

Generally availability of antineoplastic medicines amongst other essential medicines was very low in the public sector and there were very few institutions that had more than 50% availability in private pharmacies. There is a need for government health levy also being used for subsidisation of acquisition of oncology medicines.

These results shows that antineoplastic medicines were highly unaffordable taking into consideration the poverty datum line in Zimbabwe and the high unemployment rate. However the root cause analysis of the current prices had nothing to do with the mark-up of medicines in private and public pharmacies, as mark ups of 30 to 50% were noted during the study. It was more on the acquisition costs of the imported medicine in the supply chain. There is need of government subsidising the importation of essential medicines and availing foreign currency for pharmaceutical wholesalers and importers of medicines.

From the findings of this study where the price and affordability of antineoplastic medicines had an implication on access of medicines to the general public, more studies on availability and affordability of medicines need to be done in Zimbabwe to support policy formulation on better availability of medicines. More understanding is needed on how issues like out-pocket-payments impact accessibility. There is need of more research on alternative complementary medicines that can positively adjust the quality of life of cancer patients at a lower price. This is because the conventional medicines' low availability and low affordability as was demonstrated by this study means a great part of the population in Zimbabwe might not be accessing the conventional antineoplastic medicines.

There is a need for an objective, transparent and feasible price regulation system in the medical sector in Zimbabwe. This been warranted by the current unregulated market which might have an implication on the price and hence MPRs of medicines. From this study it was also evident there is need of prescribed policies that guides acquisition of medicines within government institutions and as per set approved IRP in public institutions.

Both the private sector and public sector should make us of pooled procurement and cut out the middlemen normally the wholesalers whom sometimes might have exclusive distributorship rights with manufacturers. There is a need for a review of policies on distributorship rights in Zimbabwe to increase access to medicines. There is need of ensuring that the applicants of medicines in Zimbabwe are manufacturers rather than distributors. This eliminates monopoly and hence increase competition.

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MANUSCRIPT

Price, availability and affordability of antineoplastic medicines in Harare's public and private institutions: Implication for access

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Summary

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Abstract

Background: Few studies have been conducted on price, availability and affordability of antineoplastic medicines. In Zimbabwe, there are currently no government policies on pricing and accessibility of antineoplastic medicines in public and private institutions, as is the case with HIV/AIDS medicines, antimalarial and anti-tuberculosis medicines. This is despite an annual cancer incidence of 7165 in Zimbabwe. Study was conducted on a background of better characterization of the cancer disease in the 20th century and advent of newer therapies that might be costly and whose therapeutic benefit cannot be supported clinically.

Aim: To determine the price, availability and affordability of antineoplastic medicines in Harare's public and private institutions.

Setting: Private and public sector pharmacies in Harare and Chitungwiza, Zimbabwe

Methods: The study was based on the standardised methodology recommended by the World Health Organisation (WHO) and Health Action International (HAI). A cross-sectional survey was conducted in public and private medicine outlets for thirty two (29) antineoplastic medicines. A total of 153 facilities were surveyed. These consisted of three (3) Central Hospitals and one hundred and fifty (150) private pharmacies. The percentage availability, Median Price Ratio (MRP) using International Reference Prices (IRPs), mark-ups, price and affordability of antineoplastic medicines were determined.

Results: The percentage availability of the antineoplastic medicines at the government institutions was 28%, whilst the percentage availability of the antineoplastic medicines in the private sector ranged from 1.3% to 42.7%. Fifty percent of the twenty-two (22) medicines in the private sector had a median price ratio of lower than 4. The median price ratio in the private sector ranged from 0.6 to 11. The median price ratio in the public sector ranged from 0.73 to 2.25. Eleven (11) of the medicines in the private sector were affordable with ten (10) days wage and below. Eight of the medicines were slightly affordable with wage days more than 10 days. Wage days in private sector ranged from 1 day to 490 days. Affordability of the medicines in the public sector ranged from 1 to 10 days wage. The average percentage mark-up was 51.3% in the private sector and 34% in the public sector for the medicines that were available.

Conclusion

Medicines were generally more available in the private sector than in the public sector.

Generally medicines were more affordable in the public sector than in the private sector. The average percentage mark-ups for antineoplastic medicines were 51.3% in private pharmacies and 34% in the public sector.

From the study it was evident that medicines in the private sector were sold at higher prices than the IRP and hence the price had a negative impact on availability. Medicines were generally not very affordable for the greater part of the population.

Keywords: Affordability, Antineoplastic medicines, Medicines availability, Price

Introduction

One of the Millennium Development Goals (MDGs) acknowledges the need to improve the availability of affordable medicines for all people in developing countries (WHO/HAI, 2008). This goal has been adopted into goal number 3 on good health well-being of the Sustainable Development Goals (United Nations, 2015).[1] In Zimbabwe many initiatives have been put in place through the Global Fund that mainly looks into three main 'major' diseases, that is HIV/AIDs, malaria and tuberculosis.[2] No major initiatives have been put in place to alleviate the burden of cancer treatment and palliative services.

According to the national cancer strategy of the Ministry of Health and Child Care, Zimbabwe has a cancer incidence of approximately 7145 cases per annum. The country's cancer treatment and palliation services are unable to meet the demand for services. The National Cancer control program identified low funding as one of the challenges[3]. The country with a population of 14 million people has a national poverty datum line of USD590.7 for a family of five people[4]. The majority of Zimbabweans live below the poverty datum line and this has an impact on accessibility of antineoplastic medicines.

According to Mendis et al., patients with chronic diseases require a reliable supply of affordable medicines. In the absence of such a supply, avoidable mortality and morbidity will increase. There is a need for supply of safe, efficacious and good quality antineoplastic medicines for cancer patients to reduce the disease burden in the population.

Zimbabwe does not regulate medicine prices. This can negatively impact the availability and affordability of essential medicines, like antineoplastic medicines.[5] In developing countries there is a tendency of medicine price inflation, medicine price transparency issues, and medicine price uniformity in an unregulated medicines market. In South Africa, the single exit price legislation that was introduced has addressed each of these issues by reducing medicine price inflation, improving medicine price transparency, and ensuring patients pay the same price for medicines irrespective of point of access.[6] However the introduction of the SEP has not yielded the desired outcomes of reduced medicine inflation and medicine price uniformity and there was a need for more research to see if implemented government policies yielded the desired outcomes.[7]

Studies conducted in Swaziland[7], Zimbabwe[8] and India[9] to assess the cost availability and affordability of antineoplastic medicines have showed that generally there is low availability of essential medicines in public institutions as compared to private institutions.

In Zimbabwe there is currently no essential medicines list that incorporates the antineoplastic medicines in detail.[9] This brings about variability in palliative care and can result in high out - of-pocket costs to patients.

A study was therefore done to explore prices, availability and affordability of antineoplastic medicines in Harare's private and public health institutions.

Methods

Study type

Quantitative cross-sectional survey based on the WHO/HAI method.[10]

Study setting and sampling

The study was conducted in Harare the capital city of Zimbabwe and the surrounding small towns and areas. Harare has a nearby town called Chitungwiza which is 25km away from the Central Business District. There are 250 private pharmacies and 3 public hospitals in the study setting.

Study sample

The cross sectional survey was conducted in public and private medicine outlets. A total of one hundred fifty three (153) facilities were surveyed. These consisted of three (3) central hospitals and one hundred and fifty (150) private pharmacies[11]. The percentage availability, median price ratio using international reference prices (IRPs) mark-ups, price and affordability of antineoplastic medicines were determined[12].

Sampling

Multi-stage random sampling and convenience sampling criteria was used to sample the 150 pharmacies of the 250 pharmacies in the areas of interest. The Medicines Control Authority of Zimbabwe's premises database was used for sampling purposes[11]. All the licensed pharmacies in Harare were extracted from the database and then stratified into those from high density areas and those from low density areas. A systematic random sampling approach was then implored on the strata were those even number pharmacies on the strata were chosen. Convenience sampling was implored on the government's referral hospitals because of their low number. Stratification ensured that the health institutions were as representative of the population as is possible and eliminate the location bias. Convenience and random sampling have the advantages of being cheap and in most instances more feasible to the setting.[13]

Selection of targeted antineoplastic medicines

As shown by table below. Antineoplastic medicines that have been issued a registration certificate in Zimbabwe and those that had been imported into the country through the special import process for unregistered medicines process in the year 2018 were included into the study. The WHO (2015) International Medical Price list was used for the international reference prices.[14] Median price ratios were calculated for twenty (22) of the thirty (29) products that had been sampled in the health institutions.

Table 1 Table of surveyed medicines

Antineoplastic medicine	Median cost price in USD
Cyclophosphamide 500mg injection	9
Vincristine 1mg/ml injection	4.50
Sorafenib 200mg tablets	520
Methotrexate 2.5mg tablets	18
Tamoxifen 20mg tablets	41
Letrozole 2.5mg tablets	42.50
Vinblastine 10mg/10ml injection	50
Methotrexate25mg/5ml injection	5.78
Bicalutamide 50mg tablets	51
Paclitaxel 300mg injection	69.50
Bevacizumab 25mg injection	94
Fluoro-uracil 50mg injection	6
Anastrazole 1mg tablets	107
Oxaliplatin 50mg injection	41
Doxorubicin 50mg injection	23
Oxaliplatin 100mg injection	64.50
Cisplatin 0.5mg injection	15.75
Carboplatin 450mg injection	81.10
Paclitaxel 100mg injection	60
Goserelin 3.6mg injection	203
Carboplatin 150mg injection	69.50
Goserelin 10.8mg injection	403
Docetaxel 80mg injection	135
Vinorelbin 10mg/ml injection	220
Rituximab 100mg injection	980
Abiraterone 250mg tablets	1040
Rituximab 1400mg/11.7ml/injection	1806
Trastuzumab 440mg injection	2422

Data Collection Tool/Methodology

A data collection form-based cross sectional survey was conducted in public and private medicine outlets. The data form was administered by the investigator as a hard copy in 3 (three) public institutions and 150 private health institutions in Harare and Chitungwiza from July to September 2018.

The survey tool focused on the following areas, type of institution from which data was collected, medicine generic name, dosage form, strength, manufacturer, availability at the institution, cost price of the medicine (procurement price), selling price of the medicine, mark-ups of the medicine (selling price - cost price).

Affordability (calculated as the number of days' wage of the least paid government worker which was pegged at USD296[15]). The affordability of the medicines was calculated based on the medicine required for a month's treatment of various type of cancers as stipulated in the British National Formulary and the Digital Prescribers Registry.[16]

Average price of the medicine was calculated by finding the average price for the medicine on those institutions that had the medicine on the date of survey expressed in USD. Descriptive statistics i.e. range, median, mode and mean were calculated.

Median price ratio was calculated for all the medicines with an IRP using the following equation:

$$\frac{median\ local\ unit\ price}{international\ reference\ unit\ price}$$

Statistical Analysis

The data was subsequently exported to and analysed using International Business Machines (IBM)'s Statistical Package of the Social Sciences (SPSS) ®, version 23. With the help of a biostatistician, MRPs of the twenty two (22) medicines with IRPs, percentage mark-up, percentage availability were calculated.

Data Cleaning

For accuracy of transcription, a second person checked the numerical entries for every data sheet to verify the correctness of the data.

Data Management

To protect the identity of the pharmacy respondents and to eliminate bias, pharmacy codes were used. Whereby instead of the pharmacy names, the code was used. The data sheets were stored on a password protected computer and backed-up on a password protected hard drive and a copy was stored on the Google drive ®.

Results

Availability in Private Sector

Table 2: Availability of antineoplastic medicine in the private sector

Antineoplastic medicine	Availability N=150	Percentage Availability	Availability
Bleomycin 15 IU injection	0	0	very poorly available ≤10%
Darcabazine 200mg injection	0	0	
Imatinib 400mg tablets	1	1%	
Sorafenib 200mg tablets	2	1.3%	
Docetaxel 80mg injection	2	1.3%	
Rituximab 100mg injection	4	2.7%	
Doxorubicin 50mg injection	4	2.7%	
Methotrexate 25mg/5ml injection	6	4%	
Paclitaxel 30mg injection	6	4%	
Aberaterone 250mg tablets	6	4%	
Cyclophosphamide 500mg injection	6	4%	
Carboplatin 450mg injection	8	5.3%	
Vinorelbin 10mg/ml injection	8	5.3%	
Paclitaxel 100mg injection	8	5.3%	
Rituximab 11.7mg/injection	10	7%	
Paclitaxel 300mg injection	12	8%	
Oxaliplatin 50mg injection	12	8%	
Cisplatin 0.5mg injection	14	9.3%	
Oxaliplatin 100mg injection	22	9.8%	
Bevacizumab 25mg injection	16	10.7%	poorly available 10.1%-20.9%
Trastuzumab 440mg injection	16	10.7%	
Vinblastine 10mg/10ml injection	16	10.7%	

Carboplatin 150mg injection	20	13.3%	
Fluoro-uracil 50mg injection	20	13.3%	
Vincristine 1mg/ml injection	30	20%	
Anastrazole 1mg tablets	30	20%	
Letrozole 2.5mg tablets per 30	32	21%	fairly available 21%-29.9%
Goserelin 3.6mg injection	34	26.7%	
Tamoxifen 20mg per 30 tablets	40	26.7%	
Goserelin 10.8mg injection	44	29.3%	
Bicalutamide 50mg tablets	48	32%	better available 30-50%
Methotrexate 2.5mg tablets	64	42.7	

Sixteen (19) of the thirty two (32) medicines were very poorly available in private sector with an availability of less than 10%. Seven (7) of the thirty two (32) medicines were poorly available with an availability of greater than 10% but less than 21%. Four (4) of the thirty two (32) medicines had a fairly available status. Two (2) of the thirty two (32) medicines namely Bicalutamide 50mg tablets and Methotrexate 2.5mg tablets had better availability of between 30% and 50%. Average percentage availability was 12.38% for the sampled medicines in Harare's private pharmacies.

Availability in public sector

Table 3: Availability of antineoplastic medicine in the public sector

Antineoplastic medicine	Availability N=1	Availability
Methotrexate 25mg/5ml injection	Yes	Available
Cyclophosphamide 200mg injection	Yes	
Doxorubicin 50mg injection	Yes	
Carboplatin 450mg injection	Yes	
Paclitaxel 300mg injection	Yes	
Vincristine 1mg/ml injection	Yes	
Bleomycin 15 IU injection	Yes	
Darcabazine 200mg injection	Yes	
Docetaxel 80mg injection	No	Unavailable
Rituximab 100mg injection	No	
Paclitaxel 30mg injection	No	
Aberaterone 250mg tablets	No	
Methotrexate 2.5mg tablets	No	
Vinorelbin 10mg/ml injection	No	
Paclitaxel 100mg injection	No	
Rituximab 11.7mg/injection	No	

Oxaliplatin 50mg injection	No	
Cisplatin 0.5mg injection	No	
Oxaliplatin 100mg injection	No	
Bevacizumab 25mg injection	No	
Sorafenib 200mg tablets	No	
Trastuzumab 440mg injection	No	
Vinblastine 10mg/10ml injection	No	
Carboplatin 150mg injection	No	
Fluoro-uracil 50mg injection	No	
Anastrazole 1mg tablets	No	
Letrozole 2.5mg tablets	No	
Goserelin 3.6mg injection	No	
Tamoxifen 20mg tablets	No	
Imatinib 400mg tablets	No	
Goserelin 10.8mg injection	No	
Bicalutamide 50mg tablets	No	

At Parirenyatwa hospital eight (8) of the thirty two (32) surveyed medicines were available. This represented a total of 25% medicines availability.

Median price ratio for the private sector pharmacies

Table 4 Median Price ratio for the private sector pharmacies

Product Description	International reference price in USD	Local median price in USD	Median price ratio
Cisplatin 0.5mg injection	0.515 price per ml	0.315 price per ml	0.6
Oxaliplatin 100mg injection	74.7676 price per vial	64.5 per vial	0.86
Vinblastine 10mg/10ml injectrion	4.9762 price per vial	5 per vial	1
Cyclophosphamide 500mg injection	8.16 price per vial	9 price per vial	1.10
Methotrexate 2.5mg tablets	0.1573 price per tablet	0.18 per tablet	1.14
Rituximab 100mg injection	13.6721 price/ml	18 price/ml	1.3
Imatinib 400mg tablets	25.2098 price per tablet	35 price per tablet	1.38
Oxaliplatin 50mg injection	28.8821 price per vial	41 per vial	1.42
Vincristine 1mg/ml injection	2.5416 price per vial	4.50 price per vial	1.77
Carboplatin 450mg injection	40.3245 price per vial	81.10 per vial	2
Methotrexate25mg/5ml injection	2.6258 price per vial	5.78 per vial	2.20
Fluoro-uracil 50mg injection	0.2048 price per ml	0.6 per ml	3
Letrozole 2.5mg tablets	0.4179 price per tablet	1.42 price per tablet	3.2
Doxorubicin 50mg injection	5.4059 price per vial	23 price per vial	4.2
Paclitaxel 30mg injection	0.8754 price per ml	3.7 per ml	4.22
Carboplatin 150mg injection	16.0053 price per vial	69.5 per vial	4.34
Paclitaxel 100mg injection	11.048 price per vial	60 per vial	6

Anastrazole 1mg tablets	0.5271 price per tablet	3.56 per tablet	6.7
Bicalutamide 50mg tablets	0.2343 price per tablet	1.7 per tablet	7
Docetaxel 80mg injection	17.514 price per vial	135 price per vial	7.9
Vinorelbin 10mg/ml injection	21.965 price per vial	220 price per vial	10
Tamoxifen 20mg tablets	0.1243 price per tablet	1.37 per tablet	11

Median price ratio were calculated for 22 (twenty) of the medicines. These medicines were included on the basis of having an international reference price in the WHO's international medicines guide of 2015. 50% of the antineoplastic medicines had a medicine price ratio of lower than four (4) in the private sector. Only two medicines, Vinorelbin 10mg/ml and Tamoxifen 20mg had median price ratio greater than 10 (ten) in the private sector. The median price ratio ranged from 0.6 to 11.

Median price ratio for the public sector pharmacies

Table 5 Median price ratio for the public sector pharmacies

Product Description	International reference price in USD	Local hospital median price in USD	Median price ratio
Paclitaxel 300mg/50ml injection	0.8754 per ml	0.636 per ml	0.73
Cyclophosphamide 200mg injection	4.2070 price per vial	3.80 price per vial	0.90
Doxorubicin 50mg injection	5.4059 price per vial	5.99 price per vial	1.11
Carboplatin 450mg injection	40.3245 price per vial	47.50 per vial	1.18
Vincristine 1mg/ml injection	2.5416 price per vial	3.00 per vial	1.18
Bleomycin 15U injection	12.3210 price per vial	25.70 per vial	2.09
Methotrexate 25mg/5ml injection	2.6258 price per vial	5.90 per vial	2.25

Median Price Ratios were calculated for seven (7) of the medicines that were available in public sector. These medicines were included on the basis of having an international reference price in the WHO's international medicines guide of 2015. Two (2) of the antineoplastic medicines, Paclitaxel 300mg/50ml injection and Cyclophosphamide 200mg injection had median price ratio (MRP) of lower than one (1) in the public sector, meaning they were being sold lower than the IRP. The MRP ranged from 0.73 to 2.25 in the public sector.

Affordability in private sector

Affordability was calculated from the minimum government wage/salary of USD 296. The days' wages were calculated using the unit antineoplastic price i.e the price of unit tablet or vial. (WHO, 2018). The monthly or cycle amount of an antineoplastic medicine was considered using the standard prescribing doses for the medicines i.e $296 divided by 30 days = 9.86 day

Table 6 affordability in private sector

Antineoplastic medicine	Median Cost Price in USD	Cost for one Month supply in USD	Days wages Wage	Affordability
Cyclophosphamide 500mg injection	9	9	1 day	Affordable
Vincristine 1mg/ml injection	4.50	4.50	1 day	
Sorafenib 200mg tablets	520	35	4 days	
Methotrexate 2.5mg tablets	18	36	4 days	
Tamoxifen 20mg tablets	41	41.00	5 days	
Letrozole 2.5mg tablets	42.5	42.50	5 days	
Vinblastine 10mg/10ml injection	50	50	5 days	
Methotrexate25mg/5ml injection	5.78	50	5 days	
Bicalutamide 50mg tablets	51	51	6 days	
Paclitaxel 300mg injection	69.5	69.50	7 days	
Bevacizumab 25mg injection	94	94	10 days	
Fluoro-uracil 50mg injection	6	108	11 days	Slightly affordable
Anastrazole 1mg tablets	107	107	11 days	
Oxaliplatin 50mg injection	41	123	13 days	
Doxorubicin 50mg injection	23	125	13 days	
Oxaliplatin 100mg injection	64.5	129	13 days	
Cisplatin 0.5mg injection	15.75	157.50	16 days	
Carboplatin 450mg injection	81.10	162.20	17 days	
Paclitaxel 100mg injection	60	190	20 days	
Goserelin 3.6mg injection	203	203	21 days	Unaffordable
Carboplatin 150mg injection	69.5	251.6	26 days	
Goserelin 10.8mg injection	403	403	41 days	
Docetaxel 80mg injection	135	405	41 days	
Vinorelbin 10mg/ml injection	220	440	45 days	
Rituximab 100mg injection	980	980	100 days	Highly Unaffordable
Abiraterone 250mg tablets	1040	1040	106 days	
Imatinib 400mg tablets	1050	1050	106 days	
Rituximab 1400mg/11.7ml injection	1806	1806	184 days	
Trastuzumab 440mg injection	2422	4822	490 days	

Eleven (11) of the medicines in the private sector were affordable with ten (10) wage days and below. Eight (8) of the medicines were slightly affordable with wage days more than ten (10)

days but less than 20 days. Five (5) of the medicines had wage days more than Twenty (20) days. Five (5) of the medicines were highly unaffordable with days' wages of more than 100 days to 490 days. From the results the medicines were generally unaffordable on the patient part.

4.1.6 Affordability in the public sector

Table 7: Affordability in public sector

Antineoplastic medicine	Median Cost Price in USD	Cost for one Month supply in USD	Days wages Wage of 296 9.86 per day	Affordability
Vincristine 1mg/ml injection	3.00	3.00	1 day	Very Affordable
Cyclophosphamide 200mg injection	3.80	68.40	1 day	
Doxorubicin 50mg injection	5.99	45.32	5 days	
Methotrexate25mg/5ml injection	5.90	47.20	5 days	
Bleomycin 15U injection	25.70	77.10	8 days	
Carboplatin 450mg injection	47.50	95.00	10 days	
Paclitaxel 300mg/50ml injection	31.80	95.40	10 days	

Generally antineoplastic medicines were affordable in the public sector as compared to the private sector. All the medicines were within 10 days wage. However of the 22 medicines that were considered for the study, only nine medicines were available and affordability was calculated for 7 of the medicines. This means that regardless of the low prices at public institutions, the out of pocket fees by the patients were still considerably high as there was need to source for all the unavailable medicines in the public sector.

Percentage Mark Up

Average mark up in private sector	Average mark up in public sector
51.3%	34.0%

The average percentage mark-up in private sector was 51.3% and the range was 45% to 73%. This was derived by calculating the average mark-up, which was the difference in cost price of a medicine and the selling price of the medicines found at a facility and then the total average for the private sector was calculated. The average mark-up at the private sector was 34% and the range for the mark-up was 2% to 64%.

Discussion

The study looked at price, availability and affordability of antineoplastic medicines in Harare's public and private institutions: Implications for access in a background where there was no price regulations in Zimbabwe and general unavailability of medicines.

The objectives of the study were to understand the price of antineoplastic medicines in Zimbabwe. To calculate the affordability, percentage mark-ups and percentage availability of antineoplastic medicines in Zimbabwe's private and public sector pharmacies. The study was conducted in a background were there was unavailability of medicines price control policy and significant blame of retailers by the government that there have been profiteering. The findings from the study will assist policies such as registration status for antineoplastic medicines, government policies such as cancer levy and subsidised importation of antineoplastic medicines

The study also demonstrated the challenges that cancer patients faced when it comes to accessing medicines, as most of them were living below the poverty datum line and the wage days to acquire antineoplastic medicines were very high ranging from 1 to 490 days for them.

Medicines were generally more available in the private sector. 94% of the medicines were available in the private sector pharmacies Availability was very low in the public sector. This finding was in-line with the findings of a study by Kotwani, et al. where the mean availability of essential medicines in Dehli was 41.3% in public institutions. According to the study by Kotwani et al, medicines availability was better in the private retail pharmacies as compared to the public facilities[17]. The results also compared with the study by Zaheer Ud Din Babar et al[18]. The results of the study showed that there was 25% availability of medicines in the public sector and the median availability was higher in private institutions at 45 %. The result shows that Zimbabwe as a country still has challenges in availability of antineoplastic medicines in the public sector. More has to be done in the supply chain and policies have to be implemented to increase availability in public sector.

The median price ratios in private pharmacies of 0.6 to 11, for the 22 medicines indicated that antineoplastic medicines were considerably high in the private sector compared to the private sector which had a median price ratio which ranged from 0.73 to 2.25. The medicines which had high median price ratios were brand products that did not have cheaper alternative generics. This means antineoplastic medicines were sold 0.60 to 11 times higher compared to the international reference prices. This result tallied with the finding by Marume and Bangalee,

2016 were an MPR of 10 for essential medicines was found in the private sector. More still needs to be done to ensure that generics that cost less to the brand medicines are available for antineoplastic medicines. This can be achieved by having policies that increase accessibility of generic medicines.

Eleven (11) of the medicines in the private sector were affordable with 10 wage days and below. Eight (8) of the medicines were slightly affordable with wage days more than 10 days but less than 20 days. Five (5) of the medicines had wage days more than 20 days. Four (4) of the medicines were highly unaffordable with days wages of more than 100 days to 490 days. From the results the medicines were generally unaffordable. The unaffordability of the antineoplastic medicines results in a decrement in the quality of life of cancer patients. Government subsidise could be alternative measures to bridge the gap in affordability.

Generally antineoplastic medicines were affordable in the public sector as compared to the private sector. All the medicines were within ten (10) days' wage compared with the days' wages for private retail pharmacies which ranged from 1 day to 490 days. However of the 22 medicines that were considered for the study, only six medicines were available in public institutions. This therefore means the more expensive and highly unaffordable medicines that were not available might have contributed to the low days' wages. For those same medicines that were available at both the public and private institutions, the differences were very minimal. Cases in points were those of methotrexate 25mg/5ml injection which had a median price ratio of 5.90 for public institutions and 5.78 for private institutions. There was no significant difference between the MRP. The results shows that regardless of the low prices at public institutions, the out-of-pocket fees by the patients were still considerably high, as there was still a need to source for medicines they can't access in the public sector.

The average percentage mark-up in private sector was 51.3% and the range was 45% to 73%. Whilst the average mark-up at the public sector was 34% and the range for the mark-up was 2% to 64%. The difference in prices is explained by the differences in the operational costs. The private institutions have to cater for their overhead expenses from the profit margins from the sale of medicines. This is not the case with the public sector were some of the operational costs are subsidised and some of the medicines are donated by various donors.

Strengths and limitations of the study

The study used a worldwide WHO/HAI recognised study methodology.[10] The study sample was sufficient for a survey as it surpasses the 50 samples which is minimum for a cross

sectional survey. The study used stratification and random sampling for the samples to eliminate bias. The limitations of the study were that no major studies have been done in Zimbabwe and the region on the price and availability of antineoplastic medicines, hence background information was very limited. There was low medicine availability in the public sector which affected calculation of the median price ratio comparison between the private and public sector. Also affordability was calculated on the wage/salary of the least paid government worker, this is not representative enough in an economic environment with a greater than 60% unemployment rate. It is difficult to translate the affordability to the generally unemployed population. Also the study did not look at the differences in exit prices between the generics and brand medicines. This has an impact on the median price ratio and price differences of medicines. Some medicines could not have their median price ratio calculated as they do not have international reference prices. There is likelihood of worsening availability of antineoplastic medicines as the forex situation in Zimbabwe persists.

Recommendations

The government should resuscitate local manufacturing industry and facilitate registration of generic antineoplastic medicines by local pharmaceutical manufacturers. Continued positive strides in government procurement should be commended. However the role of health economists should be implored so that cost minimisation is not the only considered means of procurement but cost effectiveness is also considered. More studies needs to be done that look at the cost and availability of antineoplastic medicines on a nationwide scale. More elaborate studies need to be done that give information on the feasibility of pricing models here in Zimbabwe.

The generic medicines policy should also be used as the median prices of generic medicines tend to be low as compared to the brand medicines. The MRPs of antineoplastic medicines in Zimbabwe for both the private and public institutions have shown that the medicines are not highly priced compared to the IRP taking into consideration the fact that we are not manufacturing any of the antineoplastic medicines.

Generally availability of antineoplastic medicines amongst other essential medicines was very low in the public sector and also there were very few institutions that had more than 50% availability in private pharmacies. There is also a need for government health levy also being used for subsidisation of acquisition of oncology products so that they would be cheaper to the general public.

These results shows that antineoplastic medicines were highly unaffordable taking into consideration the poverty datum line in Zimbabwe and the high unemployment rate. However the root cause analysis of the high prices had nothing to do with the mark-up of medicines in retail and public pharmacies, as mark ups of 30 to 50% were noted during the study. It was more on the acquisition costs of the imported medicine in the supply chain.

Government needs to capacitate local industry on antineoplastic medicines dossier acquisition and manufacturing industry resuscitation so that products are manufactured locally. This reduces transport costs which also imparts on the overall cost of medicines. This also increases competition and hence reduce prices and the cost burden on the patients.

More studies on availability and affordability of medicines needs to be done in Zimbabwe to support policy formulation on better availability of medicines. There is need of more research on alternative complementary medicines that can positively adjust the quality of life of cancer patients at lower prices as compared to the conventional medicines.

There is need to ensure that there is prescribed policies that guides acquisition of medicines within prescribed government policy and approved IRP in public institutions.

Both the retail sector and public sector should implore pooled procurement and cut on the middlemen normally the wholesalers whom sometimes might have exclusive distributorship rights with manufacturer. There is need of review of policy of distributorship rights in Zimbabwe to increase access to medicines. There is need of ensuring that the applicants of medicines in Zimbabwe are manufacturers rather than distributors. This eliminates monopoly and hence increase competition.

Conclusions

The high median price ratio in the private sector means the antineoplastic medicines in Zimbabwe are relatively costly compared to other countries. This been attributed to lack of locally manufactured medicines. Government should recapitalise local manufacturers and create bilateral partnerships with outside pharmaceutical companies that are already manufacturing antineoplastic medicines so that they set up plants locally. There is need of immediate consideration of pricing models that benefits both the general public and also promote sustainability of private retail players. There is need to improve availability of medicines in public institutions and decentralization of palliative care services from the main two general hospitals. Currently the exchange rates of the USD to the RTGS are worsening by

the day this has affected affordability of medicines given people are earning in RTGS and medicines especially in the private sector are sold in USD. The high price and low availability impacted access of the antineoplastic medicines on the patients. Low availability of antineoplastic medicines in public institutions regardless of the low prices of the medicines, meant that the out of pocket fees by patients were considerably high as they still had to source for the unavailable medicines.

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Conflict of interest

This serves as a clear declaration made by the authors that there a no financial or personal relationships that may have inappropriately influenced the research and writing of this paper.

Authors Contributions

All SNM, VB and AM contributed to the conceptualisation and designing of this study. SNM collected the data and analysed the data. All authors provided edits to the draft manuscript and approved the final version.

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Appendix 1: Medicine Price Data Collection Form

Code Name for Institution……. Date…….

Institution type: Private Pharmacy ☐ Hospital ☐ Clinic ☐

Generic name, Dosage form Strength	Product Type i.e Innovator Or Generic	Manufacturer	Availability Yes or No	Price of recommended pack size	Unit price/tab	Percentage Mark-up	Days wage	

Name of Data Collector…… Signature